Patent Claims

1. Method for the determination of TSH receptor autoantibodies (TSHR-auto-ab) in a biological sample with the aid of a receptor binding assay, in which the sample is reacted with (i) a TSH receptor preparation (TSHR preparation) and (ii) labelled bovine TSH (bTSH) and in which the presence and/or amount of the TSHR-auto-ab to be determined in the biological sample is determined on the basis of the bound amount of labelled bTSH in the complex, separated from the liquid phase, of bTSH or TSHR-auto-ab with the TSHR, characterized in that the TSHR preparation used is a functional recombinant TSH receptor (rTSHR) which is bound to a solid phase with the aid of a selective antibody against the TSH receptor (anti-TSHR-ab), purified in the bound state by washing and converted in this manner into an affinity-purified immobilized rTSHR (rTSHR(imm)*.

2. Method according to Claim 1, characterized in that the functional recombinant TSH receptor used is a functional recombinant human TSH receptor (rhTSHR) and the selective antibody used is at least one monoclonal antibody against the human TSH receptor (anti-hTSHR-mab).

3. Method according to Claim 1 or 2, characterized in that the solid phase used comprises the walls of test tubes which are precoated with an animal-specific antibody for binding the anti-TSHR-ab.

4. Method according to either of Claims 2 and 3, characterized in that at least one of the monoclonal antibodies is a monoclonal antibody against the human TSH receptor (anti-hTSHR-mab), which recognizes only conformational structures of the

rhTSHR, as obtainable by the technique of immunization with a DNA construct.

5. Method according to Claim 1, 2, 3 or 4, characterized in that the receptor binding assay is carried out as a one-step assay in a test tube coated with an affinity-purified rhTSHR(imm)*, in which assay a single reaction solution is prepared by pipetting (i) the serum-containing sample and (ii) a buffer solution which contains the labelled bTSH preparation, said reaction solution is removed from the test tube after incubation for a sufficient period, the test tube is washed and the tracer bound to the walls of the test tube is measured in a manner known per se.

6. Method according to Claim 1, 2, 3 or 4, characterized in that the receptor binding assay is carried out as a two-step assay in a test tube coated with an affinity-purified rhTSHR(imm)*, in which assay, (i) in the first step, only the sample and a buffer are pipetted, incubated and then decanted and the test tubes are washed and, (ii) in the second step, a buffer solution which contains the labelled bTSH preparation is added to the test tube, the liquid phase is removed from the test tube after incubation for a sufficient period, the test tube is washed and the tracer bound to the walls of the test tube is measured in a manner known per se.

7. Method according to Claim 1 or 2, characterized in that it is carried out in automated form, the solid phase used comprising suspended particles which are coated with a selective anti-TSHR-ab, and that the preparation of the rTSHR and the sample are added in such a way that a sample solution containing said two assay components is temporarily formed.

8. Method according to Claim 6, characterized in that the labelled bTSH is added in the second step in a serum-free buffer solution.

9. Method according to any of Claims 1 to 8, characterized in that the reaction of the sample with the affinity-purified rhTSHR(imm)* is carried out in the presence of at least one antibody against human TSH (anti-hTSH-ab).

10. Method according to Claim 9, relating back to Claim 5, characterized in that the at least one antibody against human TSH is chosen so that it does not cross-react with bovine TSH.

11. Method according to any of Claims 1 to 10, characterized in that the ~~TSH~~ receptor autoantibodies to be ~~determined~~ are receptor-stimulating autoantibodies whose occurrence in a human serum is characteristic of Graves' disease.

12. Method for the determination of TSH receptor autoantibodies (TSHR-auto-ab) in a biological sample with the aid of a receptor binding assay, in which the sample is reacted with (i) a TSH receptor preparation (TSHR preparation) and (ii) labelled bovine TSH (bTSH) and in which the presence and/or amount of the TSHR-auto-ab to be determined in the biological sample is determined on the basis of the bound amount of labelled bTSH in the complex, separated from the liquid phase, of bTSH or TSHR-auto-ab, characterized in that the receptor binding assay is carried out as a two-step assay in a test tube which is coated with an affinity-purified rhTSHR(imm)* or an immobilized fusion rhTSHR, in which assay, (i) in the first step, a sample, which contains an added anti-hTSH antibody and a buffer

are pipetted and incubated, the liquid phase is then removed from the test tube and the test tubes are washed and, (ii) in the second step, a serum-free buffer solution which contains the labelled bTSH preparation is added to the test tube, the liquid phase is removed from the test tube after incubation for a sufficient period, the test tube is washed and the tracer bound to the walls of the test tube is measured in a manner known per se.

13. Reagent kit for carrying out a competitive receptor binding assay according to any of Claims 1 to 12, characterized in that, in addition to further conventional components of a reagent kit of this type, it contains at least:

(i) test tubes coated with a rhTSHR in the form of an affinity-purified immobilized rhTSHR or of an immobilized fusion TSHR,

(ii) labelled TSH or a labelled specific TSH receptor antibody in a serum-free buffer solution.

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